

**A CONTRIBUTION TO THE NATURE OF THE MONONUCLEAR
CELLS SEEN IN THE EXUDATE OF LOBAR PNEU-
MONIA ACCOMPANYING TYPHOID FEVER.**

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IN his histological study of typhoid fever Mallory¹ describes the exudation seen in a lung of a case complicated by a typical fibrinous pneumonia of the whole lower lobe in the stage of a gray hepatization. In his specimen a very few pneumococci were present, while a bacillus, morphologically like the typhoid bacillus, occurred more abundantly, and usually within the leukocytes. In the exudate were great numbers of "large phagocytic cells with irregular vesicular nuclei situated peripherally." These cells had ingested both polymorphonuclear leukocytes and red blood corpuscles. Mallory feels that these cells are endothelial leukocytes, for he observed no evidence of migration on the part of these cells. He further observed many mitotic figures in large cells seen in the alveoli. These, of course, might be epithelial as well as endothelial, but Mallory believed after his study of the primary lesions of typhoid fever that it was not unreasonable to assign the same origin to these as that of the other mononuclear phagocytes, *i. e.*, endothelium.

Pratt² found that many of the mononuclears in early pneumonia resembled closely the cells seen in the blood and classified as "transitionals." He observed some of these same cells in the blood stream. In spite of the fact that there was not an increase of these cells in the blood stream, he felt that the "transitional" cell did enter into the formation of the exudation of early lobar pneumonia.

Evans³ approached the problem of the cytology of this exudation in a different manner. He studied, by means of the indophenol blue synthesis, three specimens of lobar pneumonia which came to necropsy on the third, fourth, and fifth days of their disease respectively, together with that found in the early stages of experimental pneumonia in rabbits. Of the mononuclear cells seen in this exudate he described and classified as follows: "(1) A few typical lymphocytes. (2) A few desquamated alveolar wall epithelial cells. (3) Relatively many oxydase-containing, large mononuclears of the blood belonging to the so-called transitional-cell group of Naegeli.

¹ An Histological Study of Typhoid Fever, Jour. Exper. Med., 1898, iii, 632.

² Histology of Acute Lobar Pneumonia, Johns Hopkins Hosp. Reports, ix, 265.

³ Evans, F. A.: The Cytology of the Exudate in the Early Stages of Experimental Pneumonia, Jour. Infect. Dis., 1916, xix, 440. Experimental Study of the Mononuclear Cells of the Blood and Tissues, Arch. Int. Med., 1916, xviii, 692.

(4) Almost as many non-oxydase-containing, large mononuclears of the blood or closely related forms." Further, the injury of the leukopoietic organs by means of benzol resulted in a loss of cells in the exudation when a pneumonia was induced, although the histogenous macrophages had been spared. In the exudation in pneumonia induced in rabbits heavily stained by combined intravenous and intraperitoneal injections of lithium carmine, neither the oxydase nor the non-oxydase mononuclears contained the vital stain.⁴

Winkler, Scultze, Gierke and others have applied the indophenol blue synthesis of Ehrlich as a differential test for the recognition of cells of myeloid origin in tissues after formalin fixation. For this purpose the test has become widely recognized. It has been used by Evans upon blood smears (1 and 2) and upon exudates in his studies of the mononuclear leukocytes (3 and 4) and of the reaction of the spleen to acute infections.⁵ Forman and Warren⁶ have used it in the identification of the cell types in myelomas. For a review of the literature and a description of the technic of the application of this reaction the reader is referred to the papers by Evans. In the light of the observations cited above, a study of the cytology of the exudate in a pneumonia associated with typhoid fever by means of this reaction should prove of interest.

Lobar pneumonia accompanying typhoid infection is not of frequent occurrence, and is usually due to some secondary infection. This is a study of such a pneumonia occurring in a young man, aged twenty years. There was an involvement of the lower lobes of both lungs, which for the most part were in the stage of gray hepatization.

The specimen had been preserved in 10 per cent. formalin for about two years and a half. According to Evans, tissues over a year old have been said to give the indophenol reaction. Graham,⁷ with a decidedly modified technic, has been able to demonstrate peroxidase ferments in tissue preserved for six years. It therefore became necessary to investigate further the length of preservation of indophenol oxydase granules by formalin. The test was applied to sections from specimens of lobar pneumonia in the stage of gray hepatization which had been kept in 10 per cent. formalin several years under the same conditions as the specimens from the typhoid case under consideration. The oldest of these specimens had been preserved for six and a half years. The polymorphonuclear leukocytes in all these specimens contained the characteristic number of indophenol oxydase granules.

⁴ Observations on the Origin and Status of the So-called Transitional White Blood Cell, *Arch. Int. Med.*, 1916, xvii, 1. The Practical Significance of the Oxydase Refraction as Applied to Blood Cells, *Proc. New York Path. Soc.*, xv, 144.

⁵ Evans, F. A.: Spleen in Acute Infections, *Bull. Johns Hopkins Hosp.*, December, 1916, p. 356.

⁶ The Identification of the Cells Seen in Myelomas by Means of the Indophenol Blue Synthesis, *Jour. Can. Res.*, 1917, ii, 79.

⁷ The Oxidizing Ferment of the Myelocyte Series of Cells and its Demonstration by Alpha-naphtholpyronin Method, *Jour. Med. Research*, November, 1916, p. 231.

Unfortunately, cultures were not obtained from the lungs at the time of the autopsy. Microscopically, however, very many bacilli were present in the sections from the pneumonic areas. These resembled closely the typhoid bacillus. Rarely coccoid forms usually arranged in pairs were encountered. While no doubt other organisms were aiding in the production of the pneumonia, the reaction has been definitely influenced by the presence of the typhoid infection in the individual, and, judged by the description and drawings, is quite similar in its cytology with the case described by Mallory.

A few areas of congestion and those containing a typical fibrinous exudation were encountered, but for the most part the alveoli were filled with serum and an abundance of cells. Many of these cells were polymorphonuclear leukocytes, and in some alveoli this type of cell predominated, a few were lymphocytes, and there was an occasional plasma cell. The predominating cells, however, were large mononuclear phagocytes. Relatively a few of these cells were much larger than the others, and frequently contained particles of black and brownish pigment. From their size, morphology, and the fact that no indophenol oxydase granules were observed in them it was assumed that they were epithelial cells. The remainder of the mononuclears resembled each other in size and shape very much. The greater number of these cells contained indophenol oxydase granules. The others, however, did not. The granule-containing cells usually possessed slightly or distinctly indented and eccentrically placed nuclei. These cells had ingested many red blood corpuscles and to a less extent polymorphonuclear leukocytes. The cells of the other group of mononuclears, which did not give the oxydase reaction, were not so numerous, and apparently they presented more frequently a round or oval nucleus. Cells of this group, however, were observed with irregular nuclei.

That some of these cells may be of lymphoid origin seems probable, and, on the other hand, it does not seem unreasonable to assume, as Mallory did, that some of them are of reticulo-endothelial origin.

In this connection an observation of Graham is of interest. With his alpha-naphthol—hydrogen peroxide—pyronin technic he has noted "that the endothelial cells of the hepatic sinusoids contain larger and smaller bodies that give a typical enzymic reaction." He also observes "that in blood smears occasional cells are found that have all the appearance of the endothelial leukocytes, so-called 'large mononuclear' or 'transitional' cells, but contain a few granules reacting to the alpha-naphthol reagent." Occasionally, in the exudate in our specimen, large mononuclear cells were encountered which tend to confirm Graham's observations. A cell with an oval nucleus has been seen in whose cell body was the nucleus of an ingested polynuclear leukocyte. The cytoplasm of this cell stained a diffuse blue without the presence of definite granules. Again, cells of the same type were encountered in which only a few granules

could be seen. The suggestion of Graham seems probable that such a result is due to phagocytosis, since Winkler has shown that the leukocytic granules resist the action of ptyalin, pepsin, and trypsin even after the remainder of the cell has been broken down.

While such an explanation accounts for a certain number of these mononuclears giving an apparently positive reaction to the indophenol blue synthesis, it does not account for the great number of cells which contain an abundance of oxydase granules. These are of myeloid origin, and, like the cells seen by Pratt and Evans, are best considered as belonging to the so-called transitional-cell group. Another observation which also strengthens this view is that in the lumina of bloodvessels of this lung similar oxydase-containing mononuclears can be found.

We have here a lung in the stage of gray hepatization with an exudation almost identical in its cytology with that seen by Evans. Whether this type of exudation has been continued through the course of the pneumonia due to specific stimulation of the "transitional-cell group" or whether it is due to the stimulation by a superimposed pyogenic infection of injured leukopoietic tissues is not entirely clear. Since, however, the bone marrow in typhoid fever shows definite lesions and the production of granular myelocytes is held in abeyance the last explanation would appear the more probable.

SUMMARY. It would appear that in the exudation in lobar pneumonia accompanying typhoid fever the mononuclear cells predominate. These mononuclear cells may be classified as: (1) lymphoid cells; (2) epithelial cells which have desquamated into the air sac; (3) large mononuclear leukocytes in abundance which contain indophenol oxydase granules; (4) large mononuclear leukocytes which are not so numerous and which do not contain the granules reacting to the indophenol blue synthesis.

UNSUSPECTED SYPHILIS: A STATISTICAL STUDY.

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THE object of this paper is to present certain statistical data drawn from the Wassermann reaction as applied to 567 consecutive private patients. Most of these patients were of the well-to-do classes, and all of them were seen in consultation, which fact warrants the assumption that they exhibited, as a whole, the more serious or puzzling diseases of inner medicine. None were supposed to suffer with venereal disease.

The Wassermann tests were done by Miss Blanche Frazier, whose